Outcomes of WHO consultation on commutability

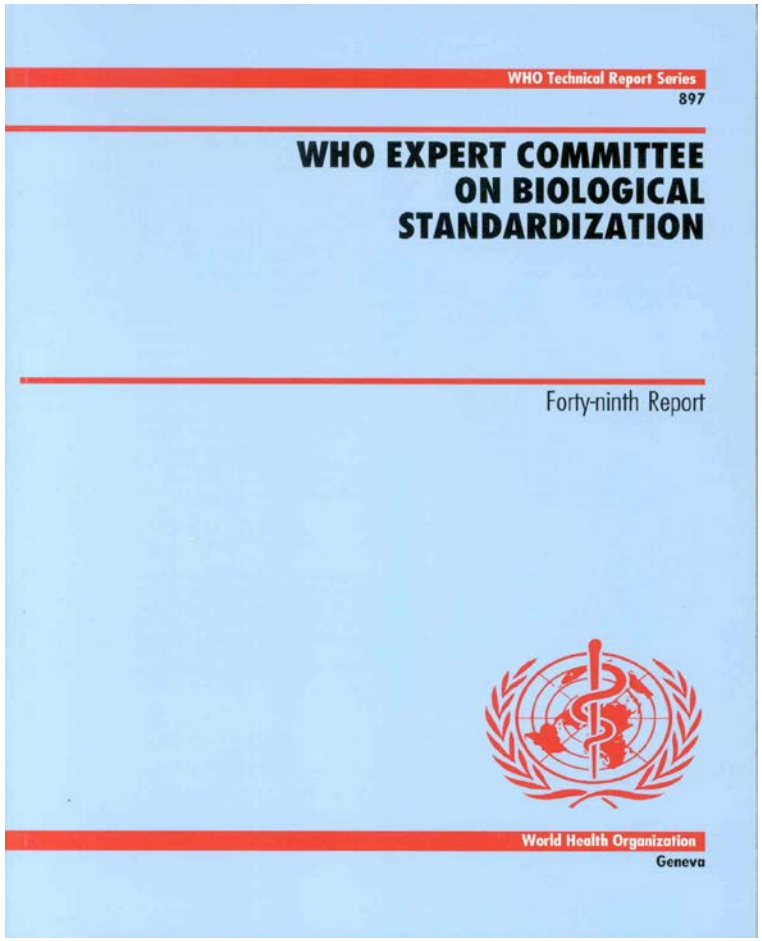
JCTLM Members and Stakeholders Meeting; Session 2
Wednesday, December 04, 2013
BIPM, Sevres, France

David Wood and Ana Padilla
TSN/EMP/HIS/WHO

World Health Organization

WHO norms and standards

Global written standards



Global measurement standards

Support to regulatory science
1) Specifications for assays
2) Standardization of QC tests
3) Scientific basis for setting specifications

Measurement standards:
tools for product development;
assay calibration; clinical dosing; licensing;
and lot release

World Health Organization

WHO technical standards - current portfo

See www.who.int/biologicals

Pharmaceutical Preparations

- approximately 75 written standards
- approximately 240 International Chemical Reference Substances
- a total of 700 specifications and test requirements in the International Pharmacopeia

Biologicals

- approximately 70 written standards
- approximately 300 international Biological Reference Substances
- scope; vaccines, biological medicines, blood products & related IVDs

WHO Consultation on Commutability of WHO Biological Reference Preparations for in vitro detection of Infectious Markers

WHO Geneva, 18-19 April 2013

50 Participants: Academia and professional organizations, Manufacturers, Regulatory Authorities and Agencies, WHO Collaborating Centres, relevant WHO programmes

WHO Consultation on Commutability of WHO Biological Reference Preparations (18-19 April 2013)

Scope:

- WHO Reference Preparations for *in vitro* detection of infectious markers
- Harmonization of *in vitro* measurements means:
  - "the same result should be obtained in a patient sample irrespective of the assay method used to derive the result for the specific measurand".
- Traceability of calibration to reference preparations needed
- “Commutable” reference preparations should behave in the same way as the measurand contained in native clinical samples.

Objectives:

To evaluate the options for assessing commutability of WHO IBRP for infectious markers

WHO Consultation on Commutability of Biological Reference Preparations

General consensus:

- Pilot studies to be performed on processing effects (e.g. dilution, inactivation, lyophilization) including multiple assays and labs
- Relevant clinical samples to be included in international collaborative studies
- Use of EQA studies where feasible or helpful
- Formal studies of commutability when technically and logistically feasible.
- Enhance written information accompanying international reference preparations
- Cooperation needed on availability of clinical samples
- Cooperative effort to be established with the AACC initiative for harmonization of clinical laboratory tests results.
- Funding opportunities to be sought among stakeholders

Recommendations on commutability of future WHO IS for NAT techniques for the detection of infection disease markers

Commutability issues may be relevant for standards in clinical virology

Commutability to be addressed, either before, during or after collaborative study

- Number of clinical samples
- Features of clinical samples (genotype, viral titre, …)
- Selection of assays (market share, technology,…)
- Link to EQA schemes

Potential commutability aspects to be considered during design of WHO IS

- WHO IS as close to clinical specimens as possible
- Effect of manipulation steps
- Pilot study

WHO Expert Committee on Biological Standardization

- 2013 ECBS reviewed the outcomes of the WHO meeting (April 2013) on commutability
- Agreed on the need to update current WHO guidance

  - "Guidelines for the preparation, characterization and establishment of International Standards and Reference Reagents"

  - WHO Technical Report Series 932 (2006)

Proposals to the Committee (2013)
II. WHO Biological Reference Preparations

- New projects endorsed:
  - Replacement of HCV RNA for NAT assays (5th IS)
  - Anti-Cytomegalovirus IgG
  - Malaria (*Pl Falciparum*) antibody reference panel
  - Sensitivity standards for cancer gene mutation detection assays
  - High and Low titre anti-A and anti-B in serum/plasma
  - Anti-Rubella Immunoglobulin
  - Replacement of Anti-Tetanus Immunoglobulin (2nd IS)
  - Assignment of FIX antigen value to 4th IS/5thFIX plasma/concentrate
  - Replacement of Ancrod (2nd IS)
  - Replacement of Streptokinase (4th IS)

Regulatory science

integration of researchers
and innovators into standardization
through regulatory science

"While it is commonly believed that standards obstruct innovation, the evidence suggests a rather different story.
Surveys of innovating firms find many enterprises say that standards are a source of information that helps their innovation activities"

From: The Economics of Standardization: An Update
G.M. Peter Swann

Further information

- www.who.int/biologicals
- www.who.int/bloodproducts
- www.who.int/medicines